I. Claims 1-14, drawn to methods of treating ischemic disorders with selectin antagonists;

II. Claims 15-28, drawn to methods of treating ischemic disorders with carbon monoxide gas;

III. Claims 29-38, drawn to methods of treating ischemic disorders with inactivated Factor IX;

IV. Claims 39-42, drawn to methods of identifying a compound capable of improving ischemia in animal models comprising a P-selectin antagonist; and

VI. Claims 43-45, drawn to methods of identifying a compound capable of preventing WBC accumulation in animal models with various inhibitors.

In the middle of page 2 of the May 5, 1997 Office Action, the Examiner stated that inventions I, II, III, IV, V and VI are different methods of use. The Examiner stated that these inventions require different ingredients, process steps and endpoints. The Examiner stated that, therefore, they are novel and unobvious in view of each other and are patentably distinct. The Examiner stated that because these inventions are distinct for the reasons given above and the search required for any group from Groups I-VI is not required for any other group from Groups I-VI and Groups I-VI have acquired a separate status in the art as shown by their different classification (and the searches are not co-extensive) and divergent subject matter, restriction for examination purposes as indicated is proper.

In section 4 at the bottom of page 2 of the May 5, 1997 Office Action, the Examiner stated that this application contains claims directed to the following patentably distinct species of the claimed invention I, wherein the selectin antagonist is:

A) a peptide mimetic;
B) a nucleic acid molecule;
C) a ribozyme;
D) a polypeptide;
E) a small molecule;
F) a carbohydrate, monosaccharide, or oligosaccharide;
G) an antibody;
H) nitroglycerin;
I) an agent which stimulates the nitric oxide pathway;
J) an agent which stimulates adenosine 3',5'-cyclic monophosphate;
K) an agent which stimulates cyclic AMP; or
L) an agent which stimulate cyclic GMP.

The Examiner stated that these species are distinct because their structures and modes of action are different. The Examiner stated that applicant is required under 35 U.S.C. § 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. The Examiner stated that, currently, claim 1 is generic.

At the top of page 3 in section 5 of the May 5, 1997 Office Action, the Examiner stated that in addition to electing a species from section 4 above, this application contains claims directed to the following patentably distinct species of the claimed invention I, wherein the selectin specificity is:

A) P-selectin;
B) E-selectin; or
C) L-selectin.

The Examiner stated that these species are distinct because their structures, expression and modes of action are different. The Examiner stated that applicants are required under 35 U.S.C. §

121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. The Examiner stated that, currently, claim 1 is generic.

In section 6 at the middle of page 3 of the May 5, 1997 Office Action, the Examiner stated that this application contains claims directed to the following patentably distinct species of the claimed invention VI, wherein the compound is:

A) a P-selectin inhibitor;
B) a monocyte inhibitor;
C) a platelet inhibitor; or
D) a neutrophil inhibitor.

The Examiner stated that these species are distinct because their structures, modes of action and targets are different. The Examiner stated that applicants are required under 35 U.S.C. § 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. The Examiner stated that currently, claim 43 is generic.

The Examiner stated that applicants are advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. The Examiner stated that an argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The Examiner stated that upon the allowance of a generic claim, applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim

as provided by 37 C.F.R. § 1.141. The Examiner stated that if claims are added after the election, applicants must indicate which are readable upon the elected species, citing M.P.E.P. § 809.02(a).

The Examiner stated that should applicants traverse on the ground that the species are not patentably distinct, applicants should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. The Examiner stated that, in either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 C.F.R. § 103 of the other invention. The Examiner advised applicants that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

In response, applicants hereby provisionally elect with traverse to prosecute the invention of Group III, i.e. claims 29-38, drawn to methods of treating ischemic disorders with inactivated Factor IX.

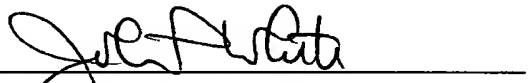
However, applicants respectfully request that the Examiner reconsider and withdraw the restriction requirement and examine Groups I, II, III, IV and VI (Groups I-VI) together in view of the following remarks. 35 U.S.C. § 121 states "[i]f two or more independent *and* distinct inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions" (emphasis added). Contrary to the requirement of 35 U.S.C. § 121, the Examiner has found that the inventions are distinct without also finding them to be independent inventions. In fact, the claims of Groups I-VI are dependent (related) inventions. In defining the term "related," the M.P.E.P. states, "the term 'related' is used as an

alternative for 'dependent' in referring to subjects other than independent subjects." M.P.E.P. § 802.01. Groups I-VI are dependent since all involve *methods related to ischemia*. Therefore, applicants respectfully assert that two or more independent *and* distinct inventions have not been claimed in the subject application because the groups are not independent under M.P.E.P. § 802.01. Accordingly, applicants contend that restriction is improper under 35 § U.S.C. 121. Further, applicants respectfully point out that under M.P.E.P. § 803, the Examiner must examine the application on the merits, even if it includes claims to distinct inventions, if the search and examination of an application can be made without serious burden. There are two criteria for a proper requirement for restriction, namely: (1) the invention must be independent and distinct; and (2) there must be a serious burden on the Examiner if restriction is not required. Applicants contend that there would not be a serious burden on the Examiner if restriction is not required. This is so because a search of the prior art for subject matter defined by claims in any one of Groups I-VI would necessarily overlap and possibly identify art pertaining to the subject matter defined by claims in any of the other Groups. For example, a search of the prior art for a method of treating ischemia with a selectin antagonist (Group I, claims 1-14) would necessarily overlap and possibly identify art pertaining to a method of treating ischemia with an inactivated Factor IX (Group III, claims 29-38). Therefore, it would not be a serious burden for the Examiner to examine all of the groups (Groups I-VI) together. Accordingly, in view of the foregoing remarks, applicants respectfully request that the Examiner reconsider and withdraw the restriction requirement and examine all of the claims in Groups I-VI together, namely claims 1-45.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

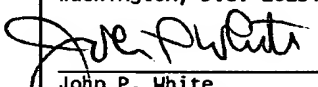
No fee, other than the $195.00 fee for a two month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White
Registration No. 28,678
Attorney for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Assistant Commissioner for Patents,
Washington, D.C. 20231.



7/17/97

John P. White — Date
Reg. No. 28,678